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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Hideyuki Okano

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EXAMINER

LEAVITT, MARIA GOMEZ

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/571,277	Applicant(s) OKANO ET AL.	
	Examiner MARIA LEAVITT	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-37 is/are pending in the application.
- 4a) Of the above claim(s) 1-17, 20, 23-26 and 28-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18, 19, 21, 22 and 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 March 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/16/2006; 01/11/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

Detailed Action

Status of claims. Claims 1-37 are pending. Applicants' election of Group VI drawn to claims 18, 19, 21, 22 and 27 and the species Galectin-1, in the reply filed on 11-15-2007 is acknowledged. Claims 31-37 reading on the elected invention have been added by applicants' amendment filed on 11-15-2007. Claims 1-17, 20, 23-26 and 28-30 are withdrawn from consideration as being directed to non-elected inventions pursuant to 37 CFR 1.14(b), there being no allowable generic or linking claim. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election was treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Therefore, claims 18, 19, 21, 22, 27 and 31-37 are currently under examination to which the following grounds of rejection are applicable.

Specification objection

The disclosure is objected to because of the following informalities:

At page 3, lines 17 and 20 the word "Galectin" is misspelled as "GalectinGalectin-1".
Appropriate correction is required.

At page 15, last paragraph, the specification recites: "During incubation of neurospheres according to Example 1, the retrovirus-containing media were each added to the culture medium and only the cell to which infection was established were sorted with the cell sorter". The term "each" refers to the election of two or more choices. It is unclear what the term "each" refers to

in the context of this sentence as there is only one choice to elect from, i.e., the retrovirus-containing media. Appropriate correction is required.

At page 22, lines 24-25, the specification recites "It is known that in the SVZ, a part of SVZ astrocytes function as stem cells, differentiate into transit amplifying cells". The sentence is grammatically incorrect. It is unclear whether a part of the SVZ astrocytes or all of the SVZ differentiate into transit amplifying cells

Priority Date

Applicants have submitted a certified copy of the Japanese foreign document. Thus the benefit of a priority date of September 9, 2003 is granted. Therefore, prior art will be applied for the priority date of September 9, 2003.

Claim Objection

Claims 21, 27, 34 and 36 are objected to because of the following informalities: abbreviations such as SVZ and C-S should be spelled out at the first encounter in the claims. Appropriate correction is required

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

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skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The instant claims are broadly drawn to a method for enhancing *in vivo* proliferation of a neuronal stem cell comprising administration of Galectin-1. The claimed method encompasses solely one active step, i.e., administering Galectin-1. Moreover, the specification does not define the term proliferation; hence the term can broadly be interpreted as one cell that replicates into two. Additionally, the specification is silent about any effective treatment of a neurological disorder. Note that treatment of neurological disorders such as stroke due to a lack of blood supply to the brain or neurogenic shock resulting from loss of vasomotor tone is not necessarily treated by administration of stem cell proliferation whereas other neurological conditions such as Alzheimer's disease are complex pathologies characterized by partial loss of myelin, axons, and oligodendroglial cells requiring treatment by targeting various processes.

Claims 18, 19, 27 and 31- 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horie et al., (US Patent 6,890,531, Date of Issue May 10, 2005) in view of Well et al., (Cell, 1991, pp. 91-97).

Horie et al., teaches a method for treating widely divergent neurological disorders including neurodegenerative diseases such as neuropathy and nerve injury resulting from ischemia (col. 2, lines 2-3; col. 13, lines 15-24). Note that treatment of cerebral ischemia and neural degenerative disease is embraced by claim 33 and 37 of the invention. Moreover, Horie et al., discloses treatment of nerve damage resulting from central and peripheral nerve injuries due to drugs, heavy metals, alcohols, ischemia or infection, malignancy or metabolic disorders such as diabetic neuropathy, or dysfunction in kidney and others (col. 5, lines 16-26) comprising treatment of degenerating nerve tissue or apoptosis and promoting the regeneration of neurites (col. 3, lines 1-5). Additionally, Horie et al., teaches that administration of Galactin-1 can be done at the site of the nerve injury, or by oral and parenteral administration (col. 5, lines 29-30, 40-41). (Current claims 18, 19, 31-33 and 35). Though Horie et al., does not explicitly teach administration of Galactin-1 to the brain, administration of Galactin-1 at the site of the nerve injury implicitly requires administration to the brain as the nerve tissue, e.g., nerve cells or neurons, is present in the brain. Further, Horie et al., discloses mutant Galactin-1 polypeptide wherein 6 cysteine residues are cross-bridged (oxidized) with a disulfide bond(s)(col. 4, lines 47-67). (Current claims 27 and 34)

Horie et al., does not specifically disclose that Galactin-1 is involved in cell proliferation.

However, at the time the invention was made, Well et al., discloses a β galactoside-binding animal lectin, i.e., Galactin-1, which is expressed constitutively and operates in regulation of cell proliferation (p. 96, col. 1, paragraph 1; Abstract).

Based on the combined teachings of Horie et al., of the treatment of cerebral ischemia and neural degenerative disease by administration of Galactin-1, and the teachings of Well et al.,

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wherein Galactin-1 is involved in the regulation of cell proliferation, one of ordinary skill in the art would recognize that treatment of cerebral ischemia and neural degenerative disease by administration of Galactin-1 implicitly involves regeneration and remyelination from nerve injuries as well as regulation of cell proliferation. Additionally, one of ordinary skill would recognize that proliferation of neuronal stem cells, though not explicitly disclosed by the combined references, would be intrinsically necessary to the administration of Galactin-1 as Galactin-1 regulates constitutively cell division. Moreover, the recitation of the intended use in the claimed invention, namely, proliferation of neuronal stem cells, in the preamble of claims 18, 21, 32, and 36 by administration of Galactin-1 fails to impart any physical or structural property to the method of administration, thus proliferation of neuronal stem cells would reasonably be expected as the combined references of Horie and Well clearly disclose the same steps i.e., administration of Galactin-1 resulting in treatment of the claimed neurological disorders, e.g. cerebral ischemia and neural degenerative disease. There would have been a reasonable expectation of success to use the methods of enhancing cell proliferation (e.g., neuronal stem cells) *in vivo* by administration of Galactin-1 for the treatment of cerebral ischemia and neural degenerative disease as taught by Horie and Well given the results of both publications demonstrating the success of the methodology, and materials detailed in each of the disclosures

Claims 21, 22, 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horie et al., (US Patent 6,890,531, Date of Patent May 10, 2005) in view of Well et al., (Cell, 1991, pp. 91-97) as applied to claims 18, 19, 27, 31-34 and 35 above and further in view of Gage

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et al., US Patent No. 6,436,389 (Date of Issue August 20, 2002) or Taupin et al., (Neuron, 2000, pp. 385-397).

The teachings of Horie et al. and Well are outlined in the paragraphs above. The combined references fail to teach the subventricular region of the brain (SVZ).

However, at the time the invention was made, Gage et al., discloses methods for the treatment of neurodegenerative disorders including neural degenerative diseases and cerebral ischemia (e.g., focal ischemia, hypoxic-ischemic encephalopathy) (col. 20, lines 30-65; line 66) comprising stereotactically injection into the rat hippocampus of genetically modified AHPs (adult hippocampus-derived neuronal progenitor cells) (col. 28, Example 5, lines 8-22).

Moreover, Gage et al., uses the glial fibrillary acidic protein (GFAP), an astrocytic marker, to detect *in vivo* proliferation of embryonic rat primary hippocampal neural progenitor cells (e.g., the subgranular layer of the dentate gyrus (DG)) (col. 29, lines 9; col. 30, lines 1-5). Further, Gage et al., teaches that intracerebral administration of FGF-2 has been shown to stimulate neurogenesis in the adult rat subventricular region of the brain (col. 1, line 50-53) wherein neurogenesis occurs throughout adulthood (col. 17; lines 57-59). Likewise, Taupin et al., exemplifies cell division in the neurogenic regions of the rat subgranular layer and SVZ after stereotactically injection into the rat hippocampus of genetically modified AHPs The author concludes that neuronal stem/progenitor cells are undergoing cell division in the SVZ (p. 391, col. 2).

Based on the combined teachings of Horie et al., of the treatment of cerebral ischemia and neural degenerative disease by administration of Galactin-1, and the teachings of Well et al., wherein Galactin-1 is involved in the regulation of cell proliferation, one of ordinary skill in the

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art would recognize that treatment of cerebral ischemia and neural degenerative disease implicitly involve regeneration and remyelination from nerve injuries as well as regulation of cell proliferation. Additionally, one of ordinary skill would recognize that proliferation of neuronal stem cells, though not explicitly disclosed by the combined references, would be intrinsically necessary to the administration of Galactin-1. The recitation of the intended use in the claimed invention, namely, proliferation of neuronal stem cells, in the preamble of claims 18, 21, 32, and 36 by administration of Galactin-1 fails to impart any physical or structural property to the method of administration, thus proliferation of neuronal stem cells would reasonably be expected as the combined references of Horie and Well clearly disclose the same steps i.e., administration of Galactin-1 resulting in treatment of the claimed neurological disorders, e.g. cerebral ischemia and neural degenerative disease. Moreover, it would have been *prima facie* obvious for one of skill in the art, as a matter of design of choice to administer Galactin-1 to any brain region associated with the contemplated treatment of a neurological disorder in order to ameliorate said disorder in a subject, particularly because neurodegenerative diseases result from alterations of physiological regulation in nerve brain cells. There would have been a reasonable expectation of success to use the methods of enhancing cell proliferation (e.g., neuronal stem cells) *in vivo* by administration of Galactin-1 for the treatment of cerebral ischemia and neural degenerative disease as taught by Horie et al., Well et al., Gage and Taupin given the results of the publications demonstrating the success of the methodology, and materials detailed in each of the disclosures.

Conclusion

Claims 18, 19, 21, 22, 27 and 31-37 are not allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Maria Leavitt/

Maria Leavitt, PhD
Examiner, Art Unit 1633

Applicants' election **with traverse** of the following species: L-phenylalanine as recited in claims 10 and 11 is acknowledged. Claims 1-8, are withdrawn from consideration as being directed to non-elected inventions pursuant to 37 CFR 1.14(b), there being no allowable generic or linking claim.